REMARKS

The Invention

The invention features E4orf4-encoding nucleic acids, pharmaceutical compositions and expression vectors containing the same, and methods for their use.

Support for Amendments

Support for the amendments to claims 88 and 95 is found in the specification on page 22, lines 20-22, and page 30, line 27, through page 31, line 4. No new matter is introduced by these amendments.

The Office Action

Claims 61-63, 81, 85-88, 92, 93, 95, 99, and 100 are pending. Claims 81 and 85-87 are allowed. Claims 61-63 are withdrawn from consideration. Claims 88, 92, 93, 95, 99, and 100 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S.P.N. 5,994,106 and/or U.S.P.N. 5,998,205.

Rejections Under 35 U.S.C. § 102(e)

Claims 88, 92, 95, and 99 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S.P.N. 5,994,106 (hereafter "the '106 patent"). Claims 88, 92, 93, 95, 99, and 100 are rejected as being anticipated by U.S.P.N. 5,998,205 (hereafter "the '205 patent"). The Examiner states that the vectors described in each of the '106 patent and the '205 patent anticipate independent claims 88 and 95, as well as at least some of the claims that depend therefrom.

Applicants have amended claims 88 and 92 to now recite that E4 polypeptides other than an E4orf4 polypeptide are not expressed by the claimed vector. Each of the '106 patent and the '205 patent fails to describe such a vector. The '106 patent discloses only expression vectors encoding the whole E4 region of adenovirus serotype 2 under the transcriptional control of the sheep

metallothionein promoter. The '205 patent discloses the generation of conditionally replicative-competent adenoviral vectors, including vectors that include tissue-specific heterologous promoters to the E4 coding region of the adenoviral genome. Neither teaches or suggests a vector in which a heterologous promoter is operably linked to a nucleic acid encoding an E4orf4 polypeptide and not encoding any other E4 polypeptide, as is now required in amended claims 88 and 95. For the foregoing reasons, the rejection of claims 88 and 95, and claims dependent therefrom, as being anticipated by the '106 patent and the '205 patent may now be withdrawn.

Moreover, applicants submit that one skilled in the art reading the '106 and '205 patents would not be motivated to make the claimed vectors. The purpose of making the vectors described in the '106 and '205 patents was to allow production of adenoviral vectors that were defective for viral replication (see, e.g., the '106 patent, which states "[s]ince E4 contains essential gene products necessary for viral growth, the resulting E4 deletion mutant virus cannot grow in the absence of exogenously expressed E4" (Col. 13, lines 29-32)). These adenoviral vectors were made by deleting a portion of the viral genome. In order to make the viruses, however, it was necessary to provide the deleted portion under the expression of a heterologous promoter.

One would not have been motivated to make the vector of claims 88 and 95 because the prior art had already established that adenovirus lacking only E4orf4 protein expression <u>are not</u> defective for replication (see, e.g., Bridge et al., Marcellus et al., of record). Thus there would be no incentive to generate or even contemplate constructing such an expression vector.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested.

Enclosed please find a Petition to extend the period for replying to the Office action for three months, to and including March 3, 2003, and a check in payment of the required extension fee.

Applicants note that the Office Action was mailed to the incorrect address. Effective immediately, please address all communication in this application to the address provided below.

If there are any additional charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 3/3/03

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Marked-up version of the claims showing changes made

88. (Three times amended) A pharmaceutical composition comprising (i) an expression vector comprising a nucleic acid encoding an E4orf4 [a] polypeptide comprising the sequence of SEQ ID NO.: 4 and capable of inducing apoptosis, and (ii) a pharmaceutically acceptable carrier, wherein said nucleic acid is operably linked to a heterologous regulatory sequence for expression of said E4orf4 polypeptide in a mammalian cell, and wherein E4 polypeptides other than said E4orf4 polypeptide are not expressed by said vector.

95. (Three times amended) An expression vector comprising a nucleic acid encoding an E4orf4 [a] polypeptide comprising the sequence of SEQ ID NO.: 4 and capable of inducing apoptosis, wherein said nucleic acid is operably linked to a heterologous regulatory sequence for expression of said E4orf4 polypeptide in a mammalian cell, and wherein E4 polypeptides other than said E4orf4 polypeptide are not expressed by said vector.